

| | | |
|--|-------------------|-----------------|
| LIST OF REFERENCES CITED BY APPLICANT (Use several sheets if necessary) | ATTY DOCKET NO. | APPLICATION NO. |
| | 8535-068-999 | To Be Assigned |
| | APPLICANT | Berns et al. |
| | FILING DATE | GROUP |
| | November 24, 2003 | To Be Assigned |

U.S. PATENT DOCUMENTS

| *EXAMINER INITIAL | | DOCUMENT NUMBER | DATE | NAME | CLASS | SUBCLASS | FILING DATE IF APPROPRIATE |
|-------------------|-----|-----------------|----------|--------------------|-------|----------|----------------------------|
| Q | A01 | 5,789,215 | 8/4/98 | Berns et al. | | | |
| | A02 | 5,631,153 | 5/20/97 | Capecchi et al. | | | |
| | A03 | 5,627,059 | 5/6/97 | Capecchi et al. | | | |
| | A04 | 5,612,205 | 3/18/97 | Kay et al. | | | |
| | A05 | 5,487,992 | 1/30/96 | Capecchi et al. | | | |
| | A06 | 5,464,764 | 11/7/95 | Capecchi et al. | | | |
| | A07 | 5,346,818 | 9/13/94 | Schafer et al. | | | |
| | A08 | 5,175,384 | 12/29/92 | Krimpenfort et al. | | | |
| | A09 | 4,997,757 | 3/5/91 | Schiestl | | | |
| | A10 | 4,950,599 | 8/21/90 | Bertling | | | |
| | A11 | 4,859,587 | 8/22/89 | Roizman | | | |

FOREIGN PATENT DOCUMENTS

| | | DOCUMENT NUMBER | DATE | COUNTRY | CLASS | SUBCLASS | TRANSLATION |
|---|-----|-----------------|----------|---------|-------|----------|---------------|
| | | | | | | | YES NO |
| Q | B01 | EP 241 044 | 10/14/87 | Europe | | | |
| | B02 | EP 265 556 | 5/4/88 | Europe | | | |
| | B03 | EP 308 220 | 3/22/89 | Europe | | | |
| | B04 | EP 315 062 | 5/10/89 | Europe | | | |
| | B05 | EP 317 509 | 5/24/89 | Europe | | | Abstract only |
| | B06 | EP 357 127 | 3/7/90 | Europe | | | |
| | B07 | EP 374 913 | 6/27/90 | Europe | | | |
| | B08 | EP 386 766 | 9/12/90 | Europe | | | Abstract only |
| | B09 | EP 397 560 | 11/14/90 | Europe | | | |
| | B10 | EP 408 301 | 1/16/91 | Europe | | | |
| | B11 | EP 410 748 | 1/30/91 | Europe | | | |
| | B12 | EP 414 297 | 2/27/91 | Europe | | | |
| | B13 | WO 83/01176 | 4/14/83 | PCT | | | |
| | B14 | WO 87/02702 | 5/7/87 | PCT | | | |
| | B15 | WO 88/06182 | 8/25/88 | PCT | | | Abstract only |
| | B16 | WO 90/07576 | 7/12/90 | PCT | | | |
| | B17 | WO 89/12684 | 12/28/89 | PCT | | | |
| | B18 | WO 90/00616 | 1/25/90 | PCT | | | |
| | B19 | WO 90/07576 | 7/12/90 | PCT | | | Abstract only |
| | B20 | WO 90/09443 | 8/23/90 | PCT | | | |
| | B21 | WO 90/11354 | 4/10/90 | PCT | | | Abstract only |

J. Weis
8/16/03

| | | | | | |
|-----------------|----------|-----------|--|--|---------------|
| 11/1/90 | PCT | | | | |
| B22 WO 90/12880 | | | | | |
| B23 WO 91/01087 | 2/7/91 | PCT | | | |
| B24 WO 91/01140 | 2/7/91 | PCT | | | |
| B25 WO 91/02070 | 2/21/91 | PCT | | | |
| B26 WO 91/02797 | 3/7/91 | PCT | | | Abstract only |
| B27 WO 91/06667 | 5/16/91 | PCT | | | |
| B28 WO 93/04169 | 3/4/1993 | PCT | | | |
| B29 DD 284898 | 11/28/90 | Germany | | | Abstract only |
| B30 JP 63068074 | 3/26/88 | Japan | | | Abstract only |
| B31 JP 63267279 | 11/4/88 | Japan | | | Abstract only |
| B32 JP 3035784 | 2/15/91 | Japan | | | Abstract only |
| B33 FR 2615527 | 11/25/88 | France | | | Abstract only |
| B34 AU 51199/90 | 3/8/90 | Australia | | | |

OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, Etc.)

| | |
|-----|---|
| C01 | Adair et al., "Targeted homologous recombinations at the endogenous adenine phosphoribosyltransferase locus in Chinese hamster cells," <i>PNAS</i> , 86:4574-4578 (1989). |
| C02 | Bain et al., "E2A Proteins Are Required for Proper B Cell Development and Initiation of Immunoglobulin Gene Rearrangements," <i>Cell</i> , 79:885-892 (1994). |
| C03 | Baker et al., "Homologous Recombination between Transferred and Chromosomal Immunoglobulin κ Genes," <i>Molecular and Cellular Biology</i> , 8(10):4041-4047 (1988). |
| C04 | Bollag et al., "Homologous recombination in mammalian cells," <i>Annual Review of Genetics</i> , 23:199-225 (1989). |
| C05 | Camerini-Otero et al., "Right on Target," <i>The New Biologist</i> , 2(4):337-341 (1990). |
| C06 | Cepecchi, M.R., "The New Mouse Genetics: Altering the Genome by Gene Targeting," <i>Trends in Genetics</i> , 5(3):70-76 (1989). |
| C07 | Cepecchi, M.R., "Altering the Genome by Homologous Recombination," <i>Science</i> , 244:1288-1292 (1989). |
| C08 | Charron et al., "High-Frequency Disruption of the N-myc Gene in Embryonic Stem and Pre-B Cell Lines by Homologous Recombination," <i>Molecular Cell Biology</i> , 10(4):1799-1804 (1990). |
| C09 | Chen et al., "B cell development in mice that lack one or both immunoglobulin κ light chain genes," <i>EMBO Journal</i> , 12(3):821-830 (1993). |
| C10 | Chisaka et al., "Developmental defects of the ear, cranial nerves and hindbrain resulting from targeted disruption of the mouse homeobox gene HOX-1.6," <i>Nature</i> , 355:516-520 (1992). |
| C11 | Cruz et al., "Gene replacement in parasitic protozoa," <i>Nature</i> , 348:171-173 (1990). |
| C12 | Deng et al., "Reexamination of Gene Targeting Frequency as a Function of the Extent of Homology between the Targeting Vector and the Target Locus," <i>Molecular and Cellular Biology</i> , 12(8):3365-3371 (1992). |
| C13 | Deng et al., "Location of Crossovers during Gene Targeting with Insertion and Replacement Vectors," <i>Molecular and Cellular Biology</i> , 13(4):2134-2140 (1993). |
| C14 | Doetschman et al., "Targeted correction of a mutant HPRT gene in mouse embryonic stem cells," <i>Nature</i> , 330:576-578 (1987). |
| C15 | Doetschman et al., "Targeted mutation of the Hprt gene in mouse embryonic stem cells," <i>PNAS</i> , 85:8583 (1988). |
| C16 | Fell et al., "Homologous recombination in hybridoma cells: Heavy chain chimeric antibody produced by gene targeting," <i>PNAS</i> , 86:8507-8511 (1989). |
| C17 | Fenton et al., "Isotypic Exclusion of $\gamma\delta$ T Cell Receptors in Transgenic Mice Bearing a Rearranged β -Chain Gene," <i>Science</i> , 241:1089-1092 (1988). |
| C18 | Fink et al., "Gene conversion in the absence of reciprocal recombination," <i>Nature</i> , 310:728-729 (1984). |
| C19 | Gridley, T., "Insertional Versus Targeted Mutagenesis in Mice," <i>The New Biologist</i> , 3(11):1025-1034 (1991). |
| C20 | Hasty et al., "Target Frequency and Integration Pattern for Insertion and Replacement Vectors in Embryonic Stem Cells," <i>Molecular and Cellular Biology</i> , 11(9):4509-4517 (1991). |
| C21 | Hasty et al., "The Length of Homology Required for Gene Targeting in Embryonic Stem Cells," <i>Molecular and Cellular Biology</i> , 11(11):5586-5591 (1991). |
| C22 | Hasty et al., "The Role and Fate of DNA Ends for Homologous Recombination in Embryonic Stem Cells," <i>Molecular and Cellular Biology</i> , 12(6):2464-2474 (1992). |
| C23 | Hooper et al., "HPRT-deficient (Lesch-Nyhan) mouse embryos derived from germline colonization by cultured cells," <i>Nature</i> , 326:292-295 (1987). |
| C24 | Itzhaki et al., "Targeted disruption of a human interferon-inducible gene detected by secretion of human growth hormone," <i>Nucleic Acids Research</i> , 19(14):3835-3842 (1991). |

John 8/16/03

| | |
|-----|---|
| Q25 | C25 Itzhaki et al., "Targeted breakage of a human chromosome mediated by cloned human telomeric DNA," <u>Nature Genetics</u> , 2:283-287 (1992). |
| | C26 Jasin et al., "Gene targeting at the human <i>CD4</i> locus by epitope addition," <u>Genes & Development</u> , 4:157-166 (1990). |
| | C27 Jasin et al., "Homologous integration in mammalian cells without target gene selection," <u>Genes & Development</u> , 2:1353-1363 (1988). |
| | C28 Joyner et al., "Production of a mutation in mouse <i>En-2</i> gene by homologous recombination in embryonic stem cells," <u>Nature</u> , 338:153-156 (1989). |
| | C29 Kim et al., "Inactivation of the human β -globin gene by targeted insertion into the β -globin locus control region," <u>Genes & Development</u> , 6:928-938 (1992). |
| | C30 Klein, H.L., "Lack of association between intrachromosomal gene conversion and reciprocal exchange," <u>Nature</u> , 310:748-753 (1984). |
| | C31 Koller et al., "Germ-line transmission of a planned alteration made in a hypoxanthine phosphoribosyltransferase gene by homologous recombination in embryonic stem cells," <u>PNAS</u> , 86:8927-8931 (1989). |
| | C32 Koller et al., "Toward an animal model of cystic fibrosis: Targeted interruption of exon 10 of the cystic fibrosis transmembrane regulator gene in embryonic stem cells," <u>PNAS</u> , 88:107030-10734 (1991). |
| | C33 Koller et al., "Inactivating the β -microglobulin locus in mouse embryonic stem cells by homologous recombination," <u>PNAS</u> , 86:8932-8935 (1989). |
| | C34 Letsou et al., "Effect of the Molecular Nature of Mutation on the Efficiency of Intrachromosomal Gene Conversion in Mouse Cells," <u>Genetics</u> , 117:759-769 (1987). |
| | C35 Lin et al., "recombination in mouse L cells between DNA introduced into cells and homologous chromosomal sequences," <u>PNAS</u> , 82:1391-1395 (1985). |
| | C36 Lindblad-Toh, K. et al., <u>Nature Genetics</u> , 24:381-386 (2000). |
| | C37 Lowy et al., "Isolation of Transforming DNA: Cloning the Hamster aprt Gene," <u>Cell</u> , 22:817-823 (1980). |
| | C38 Lyon, M.F. et al. (eds.), <u>Genetic Variants and Strains of the Laboratory Mouse</u> , Vol. Two, Third Edition, Chapter 14 (pp. 1532-1536) entitled "Rules for Nomenclature of Inbred Strains." |
| | C39 Lyon, M.F. et al. (eds.), <u>Genetic Variants and Strains of the Laboratory Mouse</u> , Vol. Two, Third Edition, Chapter 16 (pp. 1577-1596) entitled "The Laboratory Mouse and Its Wild Relatives." |
| | C40 Mansour et al., "Disruption of the proto-oncogene <i>int-2</i> in mouse embryo-derived stem cells: a general strategy for targeting mutations to non-selectable genes," <u>Nature</u> , 336:348-352 (1988). |
| | C41 Miller et al., "Targeted integration of the <i>Ren-1D</i> locus in mouse embryonic stem cells," <u>PNAS</u> , 89:5020-5024 (1992). |
| | C42 Nabel et al., "Perspectives on Human Gene Therapy," chapter 26, pages 315-319 from <u>Annual Reports in Medicinal Chemistry</u> , Vol. 26, 1991, Academic Press. |
| | C43 Nussenzweig et al., "Allelic Exclusion in Transgenic Mice That Express the Membrane Form of Immunoglobulin μ ," <u>Science</u> , 236:816-819 (1987). |
| | C44 Pascoe et al., "Genes and functions: trapping and targeting in embryonic stem cells," <u>Biochimica et Biophysica Acta</u> , 1114:209-221 (1992). |
| | C45 Reeck et al., "Homology in Proteins and Nucleic Acids: a Terminology Muddle and a Way out of it," <u>Cell</u> , 50:667 (1987). |
| | C46 Rubnitz et al., "The Minimum Amount of Homology Required for Homologous Recombination in Mammalian Cells," <u>Molecular and Cellular Biology</u> , 4(11):2253-2258 (1984). |
| | C47 Schinkel et al., "Disruption of the Mouse <i>mdrla</i> P-Glycoprotein Gene Leads to a Deficiency in the Blood-Brain Barrier and to Increased Sensitivity to Drugs," <u>Cell</u> , 77:491-502 (1994). |
| | C48 Schwartzberg et al., "Germ-Line transmission of a <i>c-abl</i> Mutation Produced by Targeted Gene disruption in ES Cells," <u>Science</u> , 246:799-803 (1989). |
| | C49 Sedivy et al., "Positive genetic selection for gene disruption in mammalian cells by homologous recombination," <u>PNAS</u> , 86:227-231 (1991). |
| | C50 Singer et al., "Determination of the Amount of Homology Required for Recombination in Bacteriophage T4," <u>Cell</u> , 31:25-33 (1982). |
| | C51 Shen et al., "Homologous Recombination in <i>Escherichia Coli</i> : Dependence on Substrate Length and Homology," <u>Genetics</u> , 112:441-457 (1986). |
| | C52 Shinkai et al., "Restoration of T Cell Development in RAG-2-Deficient Mice by Functional TCR Transgenes," <u>Science</u> , 259:822-825 (1993). |
| | C53 Simpson, E.M. et al., <u>Nature Genetics</u> , 16:19-27 (1997). |
| | C54 Smithies et al., "Insertion of DNA sequences into the human chromosomal β -globin locus by homologous recombination," <u>Nature</u> , 317:230-234 (1985). |
| | C55 Song et al., "Accurate Modification of a chromosomal plasmid by homologous recombination in human cells," <u>PNAS</u> , 84:6820-6824 (1987). |
| | C56 Soriano et al., "Targeted Disruption of the <i>c-src</i> Proto-Oncogene Leads to Osteopetrosis in Mice," <u>Cell</u> , 64:693-702 (1991). |
| | C57 te Riele et al., "Consecutive inactivation of both alleles of the <i>pim-1</i> proto-oncogene by homologous recombination in embryonic stem cells," <u>Nature</u> , 348:649-651 (1990). |
| | C58 ten Asbroek et al., "Targeted insertion of the neomycin phosphotransferase gene into the tubulin gene cluster of <i>Trypanosoma brucei</i> ," <u>Nature</u> , 348:174-175 (1990). |
| | C59 Thomas et al., "High Frequency Targeting of Genes to Specific Sites in the Mammalian Genome," <u>Cell</u> , 44:419-428 |

QW

8/16/03

| | |
|-----------|---|
| <i>24</i> | (1986). <i>cont from p 3</i> |
| C60 | Thomas et al., "Site-Directed Mutagenesis by Gene targeting in Mouse Embryo-Derived Stem Cells," <i>Cell</i> , 51:503-512 (1987). |
| C61 | Threadgill, D.W. et al., <i>Mammalian Genome</i> , 8:390-393 (1997). |
| C62 | Uematsu et al., "In Transgenic Mice the Introduced Functional T Cell Receptor β Gene Prevents Expression of Endogenous β Genes," <i>Cell</i> , 52:831-841 (1988). |
| C63 | van der Lugo et al., "Posterior transformation, neurological abnormalities, and severe hematopoietic defects in mice with a targeted deletion of the <i>bmi-1</i> proto-oncogene," <i>Genes & Development</i> , 8:757-769 (1994). |
| C64 | van der Lugo et al., "A <i>pgk::hprt</i> fusion as a selectable marker for targeting of genes in mouse embryonic stem cells: disruption of the T-cell receptor δ -chain-encoding gene," <i>Gene</i> , 105:263-267 (1991). |
| C65 | van Deursen et al., "Targeting of the creatine kinase M gene in embryonic stem cells using isogenic and nonisogenic vectors," <i>Nucleic Acids Research</i> , 20(15):3815-3820 (1992). |
| C66 | Waldman et al., "Dependence of Intrachromosomal Recombination in Mammalian Cells on Uninterrupted Homology," <i>Molecular and Cellular Biology</i> , 8(12):5350-5357 (1988). |
| C67 | Waldman et al., "Differential effects of base-pair mismatch on intrachromosomal versus extrachromosomal recombination in mouse cells," <i>PNAS</i> , 84:5340-5344 (1987). |
| C68 | Watt et al., "Homology requirements for recombination in <i>Escherichia coli</i> ," <i>PNAS</i> , 82:4768-4772 (1985). |
| C69 | Yenofsky et al., "A mutant neomycin phosphotransferase II gene reduces the resistance of transformants to antibiotic selection pressure," <i>PNAS</i> , 87:3435-3439 (1990). |
| C70 | Zheng et al., "Gene targeting in normal and amplified cell lines," <i>Nature</i> , 344:170-173 (1990). |
| C71 | Zijlstra et al., "Germ-line transmission of a disrupted β_2 -microglobulin gene produced by homologous recombination in embryonic stem cells," <i>Nature</i> , 342:435-438 (1989). |
| C72 | Zimmer et al., "Production of chimaeric mice containing embryonic stem (ES) cells carrying a homoeobox <i>Hox 1.1</i> allele mutated by homologous recombination," <i>Nature</i> , 338:150-153 (1989). |

| | | | |
|--|-----------|-----------------|----------------|
| EXAMINER | <i>24</i> | DATE CONSIDERED | <i>8/16/04</i> |
| <p>*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.</p> | | | |



Express Mail No.: **EV 475 141 422 US**

Sheet 1 of 1

| | | |
|---|-----------------|-----------------|
| LIST OF REFERENCES CITED BY APPLICANT (Use several sheets if necessary) | ATTY DOCKET NO. | APPLICATION NO. |
| | 8535-068-999 | 10/722,661 |
| | APPLICANT | |
| | Bems | |
| FILING DATE | GROUP | |
| November 24, 2003 | 1632 | |

U.S. PATENT DOCUMENTS

| *EXAMINER INITIAL | | DOCUMENT NUMBER | DATE | NAME | CLASS | SUBCLASS | FILING DATE IF APPROPRIATE |
|-------------------|-----|-----------------|------|------|-------|----------|----------------------------|
| | A01 | | | | | | |
| | A02 | | | | | | |
| | A03 | | | | | | |
| | A04 | | | | | | |
| | A05 | | | | | | |
| | A06 | | | | | | |
| | A07 | | | | | | |
| | A08 | | | | | | |
| | A09 | | | | | | |

FOREIGN PATENT DOCUMENTS

| | | DOCUMENT NUMBER | DATE | COUNTRY | CLASS | SUBCLASS | TRANSLATION |
|--|-----|-----------------|------|---------|-------|----------|-------------|
| | | | | | | | YES NO |
| | B01 | | | | | | |
| | B02 | | | | | | |
| | B03 | | | | | | |
| | B04 | | | | | | |
| | B05 | | | | | | |

OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, Etc.)

| | | |
|----|-----|--|
| 70 | C73 | Steeg et al., Introduction of specific point mutations into RNA polymerase II by gene targeting in mouse embryonic stem cells: evidence for a DNA mismatch repair mechanism. Proc Natl Acad Sci U S A. 1990 Jun;87(12):4680-4. |
| 70 | C74 | Ellis and Bernstein, Gene targeting with retroviral vectors: recombination by gene conversion into regions of nonhomology. Mol Cell Biol. 1989 Apr;9(4):1621-7. |

| | | | |
|----------|-------------------|-----------------|----------------|
| EXAMINER | <i>Joe Walter</i> | DATE CONSIDERED | <i>8/16/06</i> |
|----------|-------------------|-----------------|----------------|

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.